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Dear Examiner Crowder,

These are the claims I mentioned when we spoke. The proposed claims all have position 332 modifications. These claims include withdrawn claims for which we would seek rejoinder, such as proposed claim 4, directed to 332 variants further comprising engineered glycoforms, and proposed claims 17 and 18. Proposed claim 17 is directed to claim 1 variants further comprising additional substitutions. Proposed claim 18 is directed to multiple position variants, all of which include the 332 position.

I am out of the office 4/2/07 through 4/9/07, but please let me know if these are acceptable and we can file them as a formal supplemental response.

thanks

**PROPOSED CLAIMS FOR USSN 10/822,231**

1. An antibody and/or immunoadhesin of a parent Fc polypeptide, said antibody and/or immunoadhesin comprising at least one amino acid modification in the Fc region of said parent Fc polypeptide at position 332, wherein said antibody and/or immunoadhesin protein exhibits altered binding to an FcγR as compared to the parent Fc polypeptide, wherein numbering is according to the EU index.
2. An antibody and/or immunoadhesin according to claim 1, wherein said altered binding is an increase in affinity of said antibody and/or immunoadhesin to FcγRIIIa.
3. An antibody and/or immunoadhesin according to claim 1, wherein said altered binding is an increase in affinity of said antibody and/or immunoadhesin to FcγRIIa.
4. An antibody and/or immunoadhesin according to of claim 1; wherein said antibody and/or immunoadhesin further comprises an engineered glycoform.
5. An antibody and/or immunoadhesin according to claim 4 wherein said engineered glycoform comprises an altered level of fucosylation or bisecting oligosaccharides as compared to the parent Fc polypeptide.
- 6 An antibody and/or immunoadhesin according to claim 4 wherein said engineered glycoform improves effector function.
7. An antibody and/or immunoadhesin according to claim 6, wherein said antibody and/or immunoadhesin effector function is selected from the group consisting of antibody dependent cell-mediated cytotoxicity (ADCC) and antibody dependent cell-mediated phagocytosis (ADCP) function as compared to the parent Fc polypeptide.

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8. An antibody and/or immunoadhesin according to claim 7, wherein said antibody and/or immunoadhesin improves ADCC in the presence of human effector cells as compared to said parent Fc polypeptide.
9. An antibody and/or immunoadhesin according to claim 8 wherein said ADCC improvement is an enhancement in potency such that the EC50 of said antibody and/or immunoadhesin is approximately 5-fold greater than that of said parent Fc polypeptide.
10. An antibody and/or immunoadhesin according to claim 8, wherein said ADCC improvement is an enhancement in potency such that the EC50 of said antibody and/or immunoadhesin is between approximately 5-fold and 1000-fold greater than that of said parent Fc polypeptide.
11. An antibody and/or immunoadhesin according to claim 8, wherein said ADCC improvement is an enhancement in efficacy such that the maximal ADCC is approximately 2-fold greater than that of said parent Fc polypeptide.
12. An antibody and/or immunoadhesin according to claim 11, wherein said antibody and/or immunoadhesin improves ADCC in the presence of mouse effector cells as compared to said parent Fc polypeptide.
13. An antibody and/or immunoadhesin according to claim 7, wherein said effector function is ADCP and said antibody and/or immunoadhesin improves ADCP as compared to said parent Fc polypeptide.
14. An antibody and/or immunoadhesin according to any of claims 1- 13 wherein said polypeptide has specificity for a target antigen selected from the group consisting of CD4, CD19, CD20, CD22, CD25, CD30, CD33, CD52, CD80, B7-1, B7-2, CLTA-4, BAFF-R, Her2/neu, EGFR, EpCAM, MUC1, GD3, CEA, CA 125, HLA-DR, TNFalpha, and VEGF.
15. An antibody and/or immunoadhesin according to any of claims 1-13 comprising wherein said modification is selected from the group consisting of 332A, 332D, 332E, 332F, 332G, 332H, 332K, 332L, 332M, 332N, 332P, 332Q, 332R, 332S, 332T, 332V, 332W, and 332Y.
16. An antibody and/or immunoadhesin according to claim 14 comprising wherein said modification is selected from the group consisting of 332A, 332D, 332E, 332F, 332G, 332H, 332K, 332L, 332M, 332N, 332P, 332Q, 332R, 332S, 332T, 332V, 332W, and 332Y.
17. An antibody and/or immunoadhesin according to claim 15 wherein said modification is selected from the group consisting of 332A, 332D, 332E, 332H, 332N, 332Q, 332T, and 332Y.
18. An antibody and/or immunoadhesin according to any of claims 1-13 further comprising at least one modification selected from the group consisting of 227E, 227G, 227K, 227Y, 228E, 228G, 228K, 228Y, 230A, 230E, 230G, 230Y, 231E, 231G, 231K, 231P, 231Y, 232E, 232G, 232K, 232Y, 233A, 233D, 233F, 233G, 233H, 233I, 233K, 233L, 233M, 233N, 233Q, 233R,

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233S, 233T, 233V, 233W, 233Y, 234A, 234D, 234E, 234F, 234G, 234H, 234I, 234K, 234M, 234N, 234P, 234Q, 234R, 234S, 234T, 234V, 234W, 234Y, 235A, 235D, 235E, 235F, 235G, 235H, 235I, 235K, 235M, 235N, 235P, 235Q, 235R, 235S, 235T, 235V, 235W, 235Y, 236A, 236D, 236E, 236F, 236H, 236I, 236K, 236L, 236M, 236N, 236P, 236Q, 236R, 236S, 236T, 236V, 236W, 236Y, 237D, 237E, 237F, 237H, 237I, 237K, 237L, 237M, 237N, 237P, 237Q, 237R, 237S, 237T, 237V, 237W, 237Y, 238D, 238E, 238F, 238G, 238H, 238I, 238K, 238L, 238M, 238N, 238Q, 238R, 238S, 238T, 238V, 238W, 238Y, 239D, 239E, 239F, 239G, 239H, 239I, 239K, 239L, 239M, 239N, 239P, 239Q, 239R, 239T, 239V, 239W, 239Y, 240A, 240I, 240M, 240T, 241D, 241E, 241L, 241R, 241S, 241W, 241Y, 243E, 243H, 243L, 243Q, 243R, 243W, 243Y, 244H, 245A, 246D, 246E, 246H, 246Y, 247G, 247V, 249H, 249Q, 249Y, 255E, 255Y, 258H, 258S, 258Y, 260D, 260E, 260H, 260Y, 262A, 262E, 262F, 262I, 262T, 263A, 263I, 263M, 263T, 264A, 264D, 264E, 264F, 264G, 264H, 264I, 264K, 264L, 264M, 264N, 264P, 264Q, 264R, 264S, 264T, 264W, 264Y, 265F, 265G, 265H, 265I, 265K, 265L, 265M, 265N, 265P, 265Q, 265R, 265S, 265T, 265V, 265W, 265Y, 266A, 266I, 266M, 266T, 267D, 267E, 267F, 267H, 267I, 267K, 267L, 267M, 267N, 267P, 267Q, 267R, 267T, 267V, 267W, 267Y, 268D, 268E, 268F, 268G, 268I, 268K, 268L, 268M, 268P, 268Q, 268R, 268T, 268V, 268W, 269F, 269G, 269H, 269I, 269K, 269L, 269M, 269N, 269P, 269R, 269S, 269T, 269V, 269W, 269Y, 270F, 270G, 270H, 270I, 270L, 270M, 270P, 270Q, 270R, 270S, 270T, 270W, 270Y, 271A, 271D, 271E, 271F, 271G, 271H, 271I, 271K, 271L, 271M, 271N, 271Q, 271R, 271S, 271T, 271V, 271W, 271Y, 272D, 272F, 272G, 272H, 272I, 272K, 272L, 272M, 272P, 272R, 272S, 272T, 272V, 272W, 272Y, 273I, 274D, 274E, 274F, 274G, 274H, 274I, 274L, 274M, 274N, 274P, 274R, 274S, 274T, 274V, 274W, 274Y, 275L, 275W, 276D, 276E, 276F, 276G, 276H, 276I, 276L, 276M, 276P, 276R, 276S, 276T, 276V, 276W, 276Y, 278D, 278E, 278G, 278H, 278I, 278K, 278L, 278M, 278N, 278P, 278Q, 278R, 278S, 278T, 278V, 278W, 280G, 280K, 280L, 280P, 280W, 281D, 281K, 281P, 281Y, 282E, 282G, 282K, 282P, 282Y, 283G, 283H, 283K, 283L, 283P, 283R, 283Y, 284E, 284L, 284N, 284T, 284Y, 285D, 285E, 285K, 285Q, 285W, 285Y, 286E, 286G, 286P, 286Y, 288D, 288E, 288Y, 290D, 290H, 290L, 290N, 290W, 291D, 291E, 291G, 291H, 291I, 291Q, 291T, 292D, 292E, 292T, 292Y, 293F, 293G, 293H, 293I, 293L, 293M, 293N, 293P, 293R, 293S, 293T, 293V, 293W, 293Y, 294F, 294G, 294H, 294I, 294K, 294L, 294M, 294P, 294R, 294S, 294T, 294V, 294W, 294Y, 295D, 295E, 295F, 295G, 295H, 295I, 295M, 295N, 295P, 295R, 295S, 295T, 295V, 295W, 295Y, 296A, 296D, 296E, 296G, 296H, 296I, 296K, 296L, 296M, 296N, 296Q, 296R, 296S, 296T, 296V, 297D, 297E, 297F, 297G, 297H, 297I, 297K, 297L, 297M, 297P, 297Q, 297R, 297S, 297T, 297V, 297W, 297Y, 298A, 298D, 298E, 298F, 298H, 298I, 298K, 298M, 298N, 298Q, 298R, 298T, 298W, 298Y, 299A, 299D, 299E, 299F, 299G, 299H, 299I, 299K, 299L, 299M, 299N, 299P, 299Q, 299R, 299S, 299V, 299W, 299Y, 300A, 300D, 300E, 300G, 300H, 300K, 300M, 300N, 300P, 300Q, 300R, 300S, 300T, 300V, 300W, 301D, 301E, 301H, 301Y, 302I, 303D, 303E, 303Y, 304D, 304H, 304L, 304N, 304T, 305E, 305T, 305Y, 313F, 317E, 317Q, 318H, 318L, 318Q, 318R, 318Y, 320D, 320F, 320G, 320H, 320I, 320L, 320N, 320P, 320S, 320T, 320V, 320W, 320Y, 322D, 322F, 322G, 322H, 322I, 322P, 322S, 322T, 322V, 322W, 322Y, 323I, 324D, 324F, 324G, 324H, 324I, 324L, 324M, 324P, 324R, 324T, 324V, 324W, 324Y, 325A, 325D, 325E, 325F, 325G, 325H, 325I, 325K, 325L, 325M, 325P, 325Q, 325R, 325S, 325T, 325V, 325W, 325Y, 326E, 326I, 326L, 326P, 326T, 327D, 327E, 327F, 327H, 327I, 327K, 327L, 327M, 327N, 327P, 327R, 327S, 327T, 327V, 327W, 327Y, 328A, 328D, 328E, 328F, 328G, 328H, 328I, 328K, 328M, 328N, 328P, 328Q, 328R, 328S, 328T, 328V, 328W, 328Y, 329D, 329E, 329F, 329G, 329H, 329I, 329K, 329L, 329M, 329N, 329Q, 329R, 329S,

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329T, 329V, 329W, 329Y, 330E, 330F, 330G, 330H, 330I, 330L, 330M, 330N, 330P, 330R, 330S, 330T, 330V, 330W, 330Y, 331D, 331F, 331H, 331I, 331L, 331M, 331Q, 331R, 331T, 331V, 331W, 331Y, 333A, 333F, 333H, 333I, 333L, 333M, 333P, 333T, 333Y, 334A, 334F, 334I, 334P, 334T, 335D, 335F, 335G, 335H, 335I, 335L, 335M, 335N, 335P, 335R, 335S, 335V, 335W, 335Y, 336E, 336K, 336Y, 337E, 337H, 337N, , wherein numbering is according to the EU index.

19. An antibody and/or immunoadhesin according to any of claims 1-13 wherein said Fc region comprises modifications selected from the group consisting of 239D/332D, 239D/332E, 239D/332N, 239D/332Q, 239E/332D, 239E/332E, 239E/332N, 239E/332Q, 239N/332D, 239N/332E, 239N/332N, 239N/332Q, 239Q/332D, 239Q/332E, 239Q/332N, 239Q/332Q, 264I/332E, 297D/332E, 297E/332E, 297S/332E, 298A/332E, 328D/332E, 328E/332E, 328H/332E, 328I/332E, 328J/332E, 328M/332E, 328N/332E, 328Q/332E, 328Q/332E, 328T/332E, 328V/332E, 330L/332E, 330Y/332E, 230A/233D/332E, 239D/264I/332E, 239D/297D/332E, 239D/298A/332E, 239D/330L/332E, 239D/330Y/332E, 239D/330I/332E, 239E/264I/332E, 239E/297D/332E, 239N/298A/332E, 239N/330L/332E, 239N/330Y/332E, 239Q/264I/332E, 264E/297D/332E, 264I/298A/332E, 264I/330L/332E, 264I/330Y/332E, 265F/297E/332E, 265Y/297D/332E, 296D/297D/332E, 296E/297D/332E, 296H/297D/332E, 296N/297D/332E, 296Q/297D/332E, 296T/297D/332E, 297D/299E/332E, 297D/299F/332E, 297D/299H/332E, 297D/299I/332E, 297D/299L/332E, 297D/299V/332E, 297D/330Y/332E, 239D/264I/298A/332E, 239D/264I/330L/332E, 239D/265F/297D/332E, 239D/265H/297D/332E, 239D/265I/297D/332E, 239D/265L/297D/332E, 239D/265T/297D/332E, 239D/265V/297D/332E, 239D/265Y/297D/332E, 239D/297D/332E/235D, 239D/297D/332E/326E, 239D/297D/332E/330Y, 239D/330Y/332E/234I, 239D/330Y/332E/235D, 239D/330Y/332E/240I, 239D/330Y/332E/264T, 239D/330Y/332E/266I, 239D/330Y/332E/326E, 239D/330Y/332E/326T, 239E/264I/330Y/332E, 265Y/297D/299L/332E, 297D/298A/330Y/332E, 297D/332E/239D/330L, 239E/264I/298A/330Y/332E, 241E/243Q/262T/264E/332E, 241E/243R/262E/264R/332E, 241E/243Y/262T/264R/332E, 241R/243Q/262T/264R/332E, 241Y/243Y/262T/264T/297D/332E, and 239D/297D/332E/330Y/241S/243H/262T/264T.

20. An antibody and/or immunoadhesin according to any of claims 1-13 wherein said antibody is a full length antibody.

21. An antibody and/or immunoadhesin according to claim 14 wherein said antibody is a full length antibody.

22. An antibody and/or immunoadhesin according to claim 21 wherein said antibody comprises a human antibody.

23. An antibody and/or immunoadhesin according to claim 1 wherein said antibody comprises a human IgG1, IgG2, IgG3, or IgG4 Fc region.

24. An antibody and/or immunoadhesin according to claim 1 wherein said antibody is an antibody fragment.

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25. A pharmaceutical composition comprising an antibody and/or immunoadhesin according to any of claims 1-13 and a pharmaceutically acceptable carrier.
26. A pharmaceutical composition comprising an antibody and/or immunoadhesin according to claim 14 and a pharmaceutically acceptable carrier.
27. A pharmaceutical composition comprising an antibody and/or immunoadhesin according to claim 18 and a pharmaceutically acceptable carrier.
28. A pharmaceutical composition comprising an antibody and/or immunoadhesin according to claim 19 and a pharmaceutically acceptable carrier.
29. A method of treating a mammal in need of said treatment, comprising administering a antibody and/or immunoadhesin protein of any of claims 1-13.
30. A method of treating a mammal in need of said treatment, comprising administering a antibody and/or immunoadhesin protein of claim 14.
31. A method of treating a mammal in need of said treatment, comprising administering a antibody and/or immunoadhesin protein of claim 18.
32. A method of treating a mammal in need of said treatment, comprising administering a antibody and/or immunoadhesin protein of claim 19.